|  |  |  |
| --- | --- | --- |
|  | Number | Percentage |
| Total number of patients | 953 |  |
| Sex:  Male  Female | 610  343 | 64%  36% |
| Median age | 61.49 | Range: 20.1-102.4 |
| Types of cancer   * Lung * GI: Colon/ stomach/ esophagus * HBP: Liver/ pancreas/ biliary tract * Uro: Kidney/ bladder/ renal pelvis * Gynae: ovary/ cervix/ uterine * Head and neck * Breast * Others | 310  69  315  61  15  56  52  75 | 32.5%  7.24%  33.05%  6.40%  1.57%  5.88%  5.56%  7.87% |

Table 1: Clinical characteristics of the patients

Table 2: Types of immunotherapy used

|  |  |  |
| --- | --- | --- |
|  | Number | Percentage |
| Pembrolizumab | 552 | 57.9% |
| Nivolumab | 309 | 32.4% |
| Atezolizumab | 77 | 8.1% |
| Durvalumab | 15 | 1.6% |
| Ipilimumab | 132 | 13.9% |

Table 3: Immune-related endocrine dysfunction

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Overall** | | | | **Age > 65** | | | **Age < 65** | | |
|  | **Total number of patients** | **Total number of event** | **Percentage** | **Median time of onset (weeks)** | **Total number of event** | **Percentage** | **Median time of onset (weeks)** | **Total number of event** | **Percentage** | **Median time of onset (weeks)** |
| **Any irED** | | | | | | | | | | |
| **Total** | 953 | 279 | 29.28% |  | 104 | 30.32% |  | 175 | 28.69% |  |
| **ICI-alone** | 580 | 155 | 26.72% |  | 66 | 27.97% |  | 89 | 25.87% |  |
| **Dual-ICI** | 132 | 46 | 34.85% |  | 11 | 29.73% |  | 35 | 36.84% |  |
| **Chemo+ICI** | 187 | 53 | 28.34% |  | 18 | 33.96% |  | 35 | 26.12% |  |
| **Targeted+ICI** | 54 | 25 | 46.30% |  | 9 | 52.94% |  | 16 | 43.24% |  |
| **Hypothyroidism** | | | | | | | | | | |
| **Total** | 953 | 171 | 17.94% | 12.55 | 65 | 18.95% | 11.72 | 106 | 17.38% | 13.22 |
| **ICI-alone** | 580 | 98 | 16.90% | 12.34 | 42 | 17.80% | 12.00 | 56 | 16.28% | 12.64 |
| **Dual-ICI** | 132 | 29 | 21.97% | 15.12 | 7 | 18.92% | 17.12 | 22 | 23.16% | 14.52 |
| **Chemo+ICI** | 187 | 25 | 13.37% | 12.31 | 8 | 15.09% | 10.11 | 17 | 12.69% | 13.35 |
| **Targeted+ICI** | 54 | 19 | 35.19% | 9.75 | 8 | 47.06% | 7.13 | 11 | 29.73% | 13.31 |
| **Hyperthyroidism** | | | | | | | | | | |
| **Total** | 953 | 59 | 6.19% | 11.36 | 23 | 6.71% | 12.84 | 36 | 5.90% | 11.75 |
| **ICI-alone** | 580 | 32 | 5.52% | 13.54 | 12 | 5.08% | 16.01 | 20 | 5.81% | 12.15 |
| **Dual-ICI** | 132 | 8 | 6.06% | 4.59 | 4 | 10.81% | 4.32 | 4 | 4.21% | 4.86 |
| **Chemo+ICI** | 187 | 15 | 8.02% | 9.13 | 6 | 11.32% | 10.50 | 9 | 6.72% | 8.22 |
| **Targeted+ICI** | 54 | 4 | 7.41% | 15.75 | 1 | 5.88% | 24.71 | 3 | 8.11% | 12.76 |
| **Primary adrenal insufficiency** | | | | | | | | | | |
| **Total** | 953 | 71 | 7.45% | 26.01 | 16 | 4.66% | 27.88 | 55 | 9.02% | 22.96 |
| **ICI-alone** | 580 | 32 | 5.52% | 28.29 | 12 | 5.08% | 27.08 | 20 | 5.81% | 29.02 |
| **Dual-ICI** | 132 | 19 | 14.39% | 25.08 | 2 | 5.41% | 31.21 | 17 | 17.89% | 24.35 |
| **Chemo+ICI** | 187 | 16 | 8.56% | 26.25 | 2 | 3.77% | 29.36 | 14 | 10.45% | 25.81 |
| **Targeted+ICI** | 54 | 4 | 7.41% | 11.25 | 0 | 0.00% | 0.00 | 4 | 10.81% | 11.25 |
| **Immune-related hyperglycemia** | | | | | | | | | | |
| **Total** | 953 | 28 | 2.94% | 19.63 | 19 | 5.54% | 18.29 | 9 | 1.48% | 22.48 |
| **ICI-alone** | 580 | 21 | 3.62% | 21.63 | 13 | 5.51% | 20.30 | 8 | 2.33% | 23.80 |
| **Dual-ICI** | 132 | 0 | 0.00% | 0.00 | 0 | 0.00% | 0.00 | 0 | 0.00% | 17.14 |
| **Chemo+ICI** | 187 | 7 | 3.74% | 13.63 | 6 | 11.32% | 13.93 | 1 | 0.75% | 11.86 |
| **Targeted+ICI** | 54 | 0 | 0.00% | 0.00 | 0 | 0.00% | 0.00 | 0 | 0.00% | 0.00 |

Table 4: univariable and multivariable analysis on factors associated with immune-related endocrine dysfunction

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | any ir-ED | | Hypothyroidism | | Primary adrenal insufficiency | | Immune-related hyperglucemia | |
|  | Univariable | Multivariable | Univariable | Multivariable | Univariable | Multivariable | Univariable | Multivariable |
| **Age category** |  |  |  |  |  |  |  |  |
| < 65 (ref) | Ref | Ref | Ref | Ref | Ref | Ref | Ref | Ref |
| > 65 | 0.92 (0.66, 1.28) | 0.94 (0.66, 1.31) | 1.04 (0.69, 1.52) | 1.07 (0.71, 1.58) | **0.41 (0.18, 0.81)** | **0.39 (0.17, 0.80)** | **3.53 (1.64, 7.60)** | **3.78 (1.73, 8.32)** |
|  |  |  |  |  |  |  |  |  |
| **Treatment category** |  |  |  |  |  |  |  |  |
| ICI alone (ref) | Ref | Ref | Ref | Ref | Ref | Ref | Ref | Ref |
| Dual ICI | 1.47 (0.98, 2.19) | 1.47 (0.97, 2.19) | 1.38 (0.86, 2.18) | 1.32 (0.81, 2.10) | **2.88 (1.55, 5.22)** | **3.25 (1.72, 5.99)** | NE | NE |
| Chemo+ICI | 1.08 (0.75, 1.56) | 1.08 (0.74, 1.55) | 0.76 (0.46, 1.20) | 0.75 (0.46, 1.20) | 1.60 (0.84, 2.95) | 1.55 (0.81, 2.87) | 1.04 (0.40, 2.36) | 1.14 (0.76, 1.78) |
| Targeted+ICI | **2.36 (1.34, 4.16)** | **2.34 (1.32, 4.14)** | **2.67 (1.44, 4.81)** | **2.54 (1.36, 4.61)** | 1.37 (0.40, 3.63) | 1.50 (0.43, 4.06) | NE | NE |
|  |  |  |  |  |  |  |  |  |
| **Site of metastasis** |  |  |  |  |  |  |  |  |
| Liver | 1.08 (0.80, 1.44) | 1.00 (0.74, 1.35) | 1.31 (0.93, 1.84) | 1.24 (0.87, 1.76) | 0.62 (0.35, 1.06) | **0.51 (0.28, 0.88)** | 0.89 (0.38, 1.94) | 1.21 (0.51, 2.71) |
| Lung | 0.91 (0.69, 1.20) | 0.92 (0.69, 1.22) | 0.96 (0.69, 1.33) | 0.97 (0.69, 1.36) | 0.69 (0.41, 1.12) | 0.68 (0.41, 1.13) | 1.16 (0.54, 2.47) | 1.15 (0.53, 2.49) |
| Adrenal/ kidney | 0.95 (0.48, 1.79) | 1.00 (0.50, 1.91) | 0.67 (0.25, 1.50) | 0.69 (0.26, 1.55) | 0.86 (0.20, 2.44) | 1.13 (0.27, 3.32) | 0.72 (0.04, 3.52) | 0.47 (0.03, 2.36) |
|  |  |  |  |  |  |  |  |  |
| **Gender** |  |  |  |  |  |  |  |  |
| Female (ref) | Ref |  | Ref |  | Ref |  | Ref |  |
| Male | 0.81 (0.61, 1.08) | 0.85 (0.72, 1.21) | 0.90 (0.64, 1.27) | 0.93 (0.67, 1.32) | 0.55 (0.34, 0.90) | 0.55 (0.33, 1.02) | 1.42 (0.64, 3.46) | 1.44 (0.65, 3.42) |